PLATONIC CANCER NEUTRALIZATION NETWORK

A Control-Theoretic Framework for Evolutionary Constraint, Dependency Trapping, Arrested Funneling, Arrested Containment, and Local Elimination of Malignancy

Hypothesis / Theoretical Framework

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Scope statement

PCNN is proposed as a research architecture, not an established cancer treatment and not a clinical recommendation. Its purpose is to integrate experimentally demonstrated phenomena—adaptive therapy, collateral sensitivity, synthetic lethality, longitudinal state observation, engineered metastatic niches, and local elimination—into a single falsifiable closed-loop control framework. Quantitative toy-model outputs generated during exploratory development are not treated here as empirical findings.

by White Rabbit Geometry (Benjamin Jason Ortlip)

Abstract

Cancer is commonly treated as a target-elimination problem, yet malignant populations are heterogeneous, adaptive, spatially distributed, and capable of changing dependency structure under therapeutic pressure. We propose the Platonic Cancer Neutralization Network (PCNN), a theoretical control architecture in which malignancy is managed as an observable, steerable dynamical system. PCNN combines five experimentally grounded ideas: (i) evolutionary constraint rather than exclusive maximization of immediate cell kill; (ii) exploitation of malignancy-induced dependency traps created by redundancy loss or state change; (iii) harvesting of transient collateral sensitivities generated during treatment adaptation; (iv) spatial funneling of disseminating malignant cells toward an engineered, observable, removable quarantine node; and (v) local elimination after both funneling and containment have been actively arrested. The proposed framework distinguishes established biological observations from new mathematical constructs. It defines tumor-state transition operators, redundancy debt, escape-harvest value, and a one-way "malignant diode" whose desired topology is high ingress, near-zero egress, finite residence time, and disposable output. PCNN does not predict a universal molecular cure. It instead asks whether diverse cancers can be repeatedly forced into bounded evolutionary and spatial states in which every viable escape creates a measurable vulnerability or locally addressable disease state. We provide explicit falsification criteria and experimental programs intended for CRISPR, organoid, evolutionary-oncology, biomaterials, liquid-biopsy, mathematical-modeling, and surgical research groups. PCNN is a general architecture whose hypotheses must be instantiated and falsified one cancer, one dissemination route, one measured state transition, and one control loop at a time. Metastatic-cell capture is explicitly not treated as a surrogate for net reduction in lethal metastatic disease.

1. Central proposition

The central PCNN proposition is that the most generalizable feature of cancer may not be a shared molecular target, but a shared control problem. A malignant population survives by maintaining closure through changing networks of replication, metabolism, signaling, repair, proteostasis, microenvironmental interaction, and spatial dissemination. Cancer evolution can increase global adaptability while simultaneously destroying local redundancy. Therapeutic pressure can then close some routes, open others, and create new conditional dependencies. The treatment objective need not therefore be limited to selecting the strongest present-tense cytotoxic intervention. It can include selection of interventions that make the next malignant state more predictable and more vulnerable.

Operational scope rule: PCNN is general at the architectural level, but every experiment must be disease-, route-, state-, and controller-specific. No pan-cancer implementation is assumed.

malignant state → redundancy loss → dependency trap → therapeutic pressure → adaptation → new dependency trap

PCNN proposes that these transitions can be placed inside a feedback loop: observe the current state, constrain its evolutionary options, funnel dangerous spatial dissemination, arrest the funnel once its capture objective is met, arrest the contained population to minimize adaptation and egress, eliminate locally, and reassess.

OBSERVE	CONSTRAIN	FUNNEL	ARREST FUNNELING	ARREST CONTAINMENT	ELIMINATE	REASSESS

→	→	→	→	→	→	↺

2. Why a control architecture is scientifically plausible

2.1 Evolutionary control already exists as an oncology strategy

Adaptive therapy explicitly treats treatment resistance as an evolutionary problem. Rather than assuming that maximum immediate kill is always optimal, adaptive protocols use tumor response to alter dose or timing and attempt to preserve competitive suppression of resistant populations. The field already has mathematical and clinical foundations, and its open questions concern observability, model selection, dosing rules, heterogeneity, and translation [1,2]. PCNN extends this logic from dose adaptation to state-transition selection: the value of an intervention includes the future state it tends to create.

2.2 Collateral sensitivity supplies directed edges

Collateral sensitivity means that adaptation or resistance to one therapy increases sensitivity to another. In ALK-mutant non-small-cell lung cancer, experimentally measured collateral-sensitivity networks contained 84 unique cycles of length 2–7; one four-node cycle was crizotinib → etoposide → paclitaxel → AUY922 → crizotinib [3]. The authors appropriately described these as theoretical cycling protocols requiring further testing. In EGFR-driven lung cancer, high-complexity barcoding in populations of approximately 120 million cells demonstrated reproducible selection of pre-existing resistant subclones under gefitinib and trametinib and showed that treatment can steer clonal composition toward exploitable states [4].

More recently, soft-tissue sarcoma experiments showed that broad-spectrum tyrosine-kinase-inhibitor resistance can be cross-resistant within class while transient vulnerabilities arise en route to resistance. Sitravatinib pretreatment induced sensitivity to infigratinib as early as day 3 in A204 cells, and sequential treatment suppressed growth in the experimental system [5]. PCNN therefore treats vulnerability as time-dependent: $V(T \mid S,t)$, not merely $V(T)$.

2.3 Redundancy loss creates dependency traps

Genome-scale dependency maps increasingly reveal conditional rather than universal vulnerabilities. A 2026 DepMap expansion performed 147 genome-scale CRISPR screens in next-generation 3D cancer models across 10 cancer types. It identified 51 strong expression addictions and 106 strong paralogue-associated dependencies; ENO1 dependence was stronger in ENO2-low next-generation models than in traditional cell lines [6]. A separate patient-derived organoid biobank linked gene fitness effects to genomic and clinical features and reported 1,841 significant gene–biomarker associations, including WRN dependency associated with mismatch-repair-deficiency/MSI-linked features such as SBS44 [7].

The normal-tissue problem is decisive. A 2025 comparative CRISPRi study targeted 151 genes classified as common essential across more than 500 cancer cell lines; 150 of 151 were also negative fitness hits in dividing non-cancer human cell systems [8]. This argues against equating universal cancer essentiality with a therapeutic window. PCNN instead prioritizes conditional dependencies created by malignant loss of redundancy.

The SMARCA4–SMARCA2 relationship illustrates this topology. SMARCA4-deficient cancers become dependent on the paralogous SWI/SNF ATPase SMARCA2. The selective SMARCA2 degrader PRT3789 produced strong preclinical activity in SMARCA4-deficient models while wild-type models showed minimal response despite SMARCA2 degradation; early clinical activity included RECIST-confirmed partial responses [9]. VPS4A/VPS4B provides another example in which chromosomal loss can delete

one paralogue and expose dependency on the remaining ESCRT ATPase [10]. MTAP deletion creates a distinct, non-paralogue metabolic dependency state exploitable through PRMT5/MTA-cooperative inhibition; in a phase I study, AMG 193 produced a 21.4% objective response rate among 42 efficacy-assessable patients at active/tolerable doses, with responses across eight tumor types [11].

3. Proposed PCNN mathematics

The equations in this section are proposed PCNN constructs unless otherwise stated. They are definitions for testing, not established laws of tumor biology.

3.1 State and control

$$x(t+1) = F[x(t), u(t), e(t)]$$

Let x(t) denote the observable malignant state, including clonal composition, molecular dependencies, burden, spatial distribution, and relevant microenvironmental variables. Let u(t) denote therapeutic or local-control actions and e(t) denote environmental and host variables. A probabilistic representation is:

$$P(S_j \mid S_i, T_k, t)$$

which is the probability that treatment T_k applied to state S_i produces state S_j at the relevant observation time. PCNN seeks policies that favor transitions into states with fewer dangerous exits and stronger exploitable dependencies.

3.2 Redundancy debt

$$D_R(F) = W_N(F) - W_C(F)$$

For functional requirement F, W_N is the number or effective weight of viable routes in the relevant normal system and W_C is the corresponding route multiplicity in the malignant state. Large positive redundancy debt means the cancer has sacrificed alternatives that normal tissue retains. A high-value dependency trap occurs when the cancer has effectively collapsed to one remaining route while normal tissue retains alternatives.

$$W_N(F) > 1, \quad W_C(F) \approx 1$$

3.3 Vulnerability operator

$$V(r,t) = D_R(r,t) \cdot E_C(r,t) \cdot P_C(r,t) / \{[1 + X_C(r,t)] \cdot [1 + C_N(r,t,h)]\}$$

Here E_C is malignant dependency strength, P_C is prevalence or recurrence of the state across the intended population, and X_C is malignant escape connectivity. Normal-tissue tolerance is not assumed static: treatment, inflammation, stromal activation, wound healing, organ injury, immune activation, and prior therapy can change host dependencies. PCNN therefore requires a concurrent host-state estimate h(t) and a conditional normal-tissue cost C_N(r,t,h). Each term requires operational definition and calibration for a given experimental system.

3.4 Escape-harvest operator

$$H(T_1,T_2,\tau \mid S_0) = V(T_1 \mid S_0) + V[T_2 \mid E(S_0,T_1,\tau)] - R - N$$

$E(S_0,T_1,\tau)$ denotes the state induced by treatment T_1 after interval τ; R penalizes rerouting capacity and N penalizes normal-tissue cost. The key prediction is that $T_1 + T_2$ and $T_1 \rightarrow T_2$ need not be therapeutically equivalent because T_2's target state may not yet exist at baseline.

3.5 Check, perpetual check, and terminal control

PCNN distinguishes eradication from bounded control. A terminal state with no viable malignant exit is the idealized "checkmate" condition. A "perpetual check" condition does not require an unlimited library of therapies. It requires a finite, reusable control subgraph - or a bounded absorbing control region - in which every clinically reachable outgoing malignant transition remains addressable by at least one available intervention. This is a graph property, not a claim that any presently known drug set already satisfies it.

$$\text{checkmate: } d^{+}(S^{*}) = 0$$

perpetual check: finite control set U^{*} keeps $S(t)$ inside bounded region B, with every viable outgoing edge from B therapeutically addressable

4. Spatial control: malignant-diode topology as a quarantine-node design objective

The spatial component asks whether disseminating malignant cells can be preferentially redirected toward engineered, observable, locally controllable destinations. PCNN does not assume a single universal trap. Hematogenous, lymphatic, transcoelomic/peritoneal, and other dissemination routes can coexist; therefore the spatial controller is better represented as a compartment-specific quarantine network $Q = \{Q_{blood}, Q_{lymph}, Q_{peritoneum}, \ldots\}$, selected according to the dominant metastatic flux and downstream establishment risk in the cancer being modeled. Engineered niches can capture disseminated tumor cells and reproduce aspects of pre-metastatic niche biology [12,13]. The ovarian-cancer M-Trap study is especially relevant: an exosome-bearing 3D scaffold became a preferential site of metastasis in mouse models, remodeled peritoneal dissemination, increased mean survival from 117.5 to 198.8 days, and, when removed after tumor capture, increased mean survival to 309.4 days in that experiment [14].

Quarantine interventions must also be evaluated against host hazards such as thrombosis, infection, inflammatory remodeling, fibrosis, angiogenesis, immune perturbation, altered drainage, procedural morbidity, and local-tissue injury. These are independent failure modes even when malignant egress is low.

4.1 The diode topology

$$\text{Primary / circulating malignancy} \rightarrow Q \rightarrow \text{local elimination}$$

$$J_Q = \Sigma_k \, \Phi_k \, P_k$$

$$\text{desired: } d_{in}(Q) \gg 0, \quad d_{out}(Q) \approx 0$$

Q is not intended to be a hospitable secondary organ. "Malignant-diode topology" names a hypothesized design objective, not an established device class: high malignant ingress, minimal egress, high observability, finite residence time, and rapid removability or ablation. A passive niche that attracts tumor cells but permits prolonged growth and reseeding fails the PCNN design. Trap placement is itself an optimization problem: prioritize compartments that account for the largest expected dangerous metastatic flux per unit of intervention morbidity rather than attempting to instrument every anatomical route.

$$Q^{*} = \arg\max_Q \left[\Delta\Lambda_{metastatic}(Q) / \text{morbidity}(Q)\right]$$

4.2 Arrested funneling

Funneling must be a controlled phase, not a permanent attractor. Once a predefined capture or safety condition is reached, the attraction mechanism should be deactivated, removed, isolated, or otherwise

rendered unable to continue recruiting malignant traffic. PCNN calls this arrested funneling. The purpose is to avoid turning the quarantine device into an indefinitely active metastatic destination.

4.3 Arrested containment

After funneling is arrested, the captured population should itself be placed into a low-growth, low-adaptation, low-egress state pending destruction or explantation. PCNN calls this arrested containment. The distinction matters: stopping recruitment does not stop the malignant population already present from evolving, vascularizing, invading, or reseeding.

4.4 Quarantine state machine

$$Q_0 \text{ inactive} \rightarrow Q_1 \text{ capture/funnel} \rightarrow Q_2 \text{ funnel arrested} \rightarrow Q_3 \text{ containment arrested} \rightarrow Q_4 \text{ removed/ablated}$$

The transition $Q_1 \rightarrow Q_1$ indefinitely is explicitly disallowed as a design goal. Each state requires measurable transition criteria and a fail-safe path to local destruction.

$$\text{malignant capture} \neq \text{metastatic benefit}$$

A quarantine node can capture large numbers of malignant cells and still worsen disease. PCNN therefore forbids use of device burden or capture efficiency alone as a therapeutic endpoint. The relevant spatial endpoint is net dangerous metastatic establishment outside the quarantine node, together with survival and host harm. A high-capture device that increases distal metastasis, viable egress, or mortality is a failed intervention.

4.5 Capture is not metastatic benefit

5. Why systemic and spatial control must be coupled

A spatial trap cannot safely compensate for unlimited dissemination. If n viable dissemination attempts occur and each has residual probability p of escaping spatial control and establishing dangerous disease, then under a simple independence approximation:

$$P(\text{containment}) = (1 - p)^n$$

$$P(\text{escape}) = 1 - (1 - p)^n$$

For small p, $(1 - p)^n \approx \exp(-np)$. The approximation is elementary probability, but its control implication is central:

$$\Lambda_\text{escape} \propto N_\text{attempts} \times P_\text{success per attempt}$$

Evolutionary constraint attacks the first factor by reducing malignant burden, viable shedding, or the number of dangerous states capable of dissemination. The malignant diode attacks the second by reducing the probability that an individual dissemination event establishes at a dangerous site. Local elimination clears accumulated captured disease. PCNN therefore does not require either systemic therapy or spatial interception to perform the impossible task alone.

6. PCNN objective function

$$\pi^* = \arg\min_\pi \; E[B + \lambda_R R + \lambda_M M + \lambda_N N + \lambda_U U + \lambda_Q H_Q]$$

B is malignant burden; R is evolutionary freedom or escape connectivity; M is dangerous spatial dispersion; N is systemic normal-tissue injury; U is uncertainty/observability penalty; and H_Q is quarantine-node host hazard, including device- or procedure-associated injury. The λ terms encode context-dependent costs. This formulation deliberately allows a treatment with lower immediate

cytoreduction to outrank a stronger cytotoxic treatment if it produces a substantially more controllable future state.

A complete implementation would be a partially observed stochastic control problem. State estimates would be updated from serial measurements such as circulating tumor DNA, imaging, circulating tumor cells, proteomic/metabolomic measurements, biopsies, or model-specific biomarkers. PCNN does not assume that one modality will be sufficient for every cancer.

7. What PCNN claims—and does not claim

PCNN proposes	PCNN does NOT presently establish
A unified closed-loop architecture connecting existing cancer-control phenomena.	A universal cure, validated clinical regimen, or patient-specific treatment recommendation.
Redundancy loss and state change as candidate sources of malignancy-specific dependency traps.	That every cancer possesses a safe, exploitable dependency trap.
Therapy sequencing as a state-transition control problem.	That any proposed drug sequence is safe or effective in humans without validation.
A removable, one-way spatial quarantine node as an engineering target.	That present biomaterial traps are ready for routine clinical use or can capture all metastatic routes.
Arrested funneling and arrested containment as explicit safety requirements.	That the mechanisms required to implement these states have already been engineered.
Falsifiable mathematical definitions and experimental programs.	Validated numerical parameter values for capture efficiency, egress, switching time, or clinical benefit.

7.1 Operationalization before optimization

Terms such as redundancy debt, escape connectivity, vulnerability, and host cost are model scaffolds until mapped to measurable variables. The first wet-lab controller should therefore be rule-based and preregistered rather than a complex latent-state optimizer. For one chosen model, define an observable state vector containing only quantities that can actually be measured at the required cadence.

$$\hat{x}(t) = \{\text{burden, clone frequencies, state biomarker, dissemination flux, quarantine burden, host-toxicity markers}\}$$

$$\text{example rule: if } z(t) > z^* \text{ for two consecutive samples, switch } T_1 \rightarrow T_2$$

8. Modular validation program

PCNN should be validated in modules before integration: state measurement → evolutionary steering → conditional dependency → spatial capture → arrest/removal → integration. Failure of an upstream module blocks claims about the downstream integrated controller.

8.1 CRISPR / organoid laboratories

Construct paired normal-versus-malignant route maps. Rank candidate vulnerabilities by redundancy debt, malignant dependency, normal-cell tolerance, prevalence, and escape connectivity. Test whether the proposed vulnerability operator enriches for known conditional dependencies (for example SMARCA4/SMARCA2, VPS4A/VPS4B, MSI/WRN) before using it prospectively to nominate previously unrecognized relationships.

8.2 Evolutionary-oncology laboratories

Generate longitudinal collateral-sensitivity graphs under multiple mechanistically orthogonal treatments. Measure transition probabilities, edge persistence, and harvest windows rather than only endpoint resistance. Compare fixed combinations, fixed sequences, and closed-loop state-triggered switching. A strong test is whether PCNN-selected steering policies outperform greedy immediate-kill policies under identical toxicity constraints. No directed edge should enter the PCNN control graph solely from mechanistic plausibility; it must be measured in the relevant model or supported by directly transferable evidence.

8.3 Biomaterials / metastasis laboratories

Treat the engineered niche as a controllable state machine rather than a passive scaffold. Measure ingress, retention, egress, reseeding competence, vascularization, and adaptation over time. Explicitly test arrested funneling and arrested containment. The central safety metric is not capture alone but net reduction in dangerous metastatic establishment after accounting for device-derived dissemination.

8.4 Liquid-biopsy / monitoring laboratories

Search for minimal signatures that classify PCNN states quickly enough to act on transient vulnerabilities. The relevant metric is control latency: measurement-to-decision time must be shorter than the persistence of the exploitable state transition. The controller must estimate both malignant state $\hat{S}_C(t)$ and host state $\hat{S}_H(t)$, because a tumor-selective dependency can lose its therapeutic window when stressed normal tissues acquire the same requirement.

$$L_{observe} + L_{infer} + L_{act} < \tau_{vulnerability}$$

8.5 Mathematical / computational oncology

Build stochastic, partially observed models with explicit normal-tissue costs and adversarial tumor branching. Perform global sensitivity analysis rather than relying on single assumed parameters. For spatial trapping, map phase boundaries over capture probability, egress, shedding, colonization probability, and harvest interval. For evolutionary steering, search for robust absorbing regions, stable cycles, and terminal low-escape funnels.

9. Falsification and failure criteria

Stopping criteria should be prespecified before experimentation. The integrated design fails if active capture increases non-device metastatic burden, if viable egress exceeds the model-specific validated ceiling, if the vulnerability window is shorter than sensing plus decision plus treatment latency, if stressed normal tissue loses selectivity, or if the integrated controller cannot outperform the best single-module/fixed-sequence control at matched toxicity.

PCNN should be treated as wrong, incomplete, or domain-limited wherever the following conditions hold. These are not caveats to be hidden; they are the intended scientific attack surface.

- Treatment-induced state transitions are too stochastic or patient-specific for useful steering after conditioning on measurable state.
- Collateral sensitivities are too weak, too short-lived, or too toxic to exploit before resistant branching occurs.
- Normal-tissue toxicity removes the therapeutic window for the dependency traps required by the controller.
- Evolutionary branching expands faster than clinically feasible observation and control can constrain it.

- The act of funneling increases dangerous dissemination or creates a new metastatic source.
- A quarantine device cannot achieve sufficiently low egress or cannot be removed/ablated before captured cells adapt.
- Arrested funneling or arrested containment cannot be implemented without unacceptable host injury.
- State observability is too slow or noisy relative to the relevant transition timescale.
- A closed-loop PCNN policy fails to outperform appropriate standard, adaptive, or combination-therapy controls in preclinical models.

10. Minimal module experiments

The first experiments should test one edge at a time. A steering module can ask whether one measured T_1-induced state is sensed quickly enough for state-triggered T_2 to outperform fixed sequencing under matched toxicity. Separately, a quarantine module can ask whether a removable engineered niche reduces total dangerous metastatic establishment after accounting for egress, reseeding, vascularization, and host injury. Only after both modules pass independently should they be combined. No generic drug pair or universal egress threshold is prescribed by PCNN.

11. Decisive preclinical integration test

A decisive integration experiment should use a metastatic, barcoded, appropriately immune-competent model with a removable engineered niche only after the steering and quarantine modules have independently passed. Establish baseline clonal and spatial state. Use a steering therapy only when the induced vulnerability has already been measured in that exact model. Activate the engineered niche only during a predefined dissemination window; once prespecified capture criteria are met, arrest funneling, arrest or locally destroy the contained population, and remove or ablate the node. Continue longitudinal monitoring.

Randomize, where feasible, among: (1) standard-of-care or matched maximum-tolerated-dose analogue; (2) T_1 alone; (3) fixed $T_1 \rightarrow T_2$; (4) state-triggered $T_1 \rightarrow T_2$ without quarantine; (5) quarantine without evolutionary steering; (6) state-triggered $T_1 \rightarrow T_2$ plus quarantine, arrest, and removal/ablation; and (7) inactive/sham-device control when scientifically and ethically appropriate. Primary outcomes should be survival or a defensible disease-specific analogue and total lethal metastatic burden across relevant organs—not device capture. Safety-critical outcomes include egress/reseeding, off-device metastatic burden, vascularization/invasion, host injury, inflammation, wound-healing effects, and procedural morbidity.

Statistical design requirements: preregister the state definition, switch threshold, latency ceiling, egress failure criterion, toxicity ceiling, primary endpoint, analysis plan, and stopping rules; randomize allocation; blind endpoint assessment where feasible; power the study on survival/metastatic burden rather than capture; and seek independent replication before treating an integrated result as support for the general architecture.

11.1 Quarantine-node risk register

Every quarantine experiment should prospectively score at least: malignant egress; reseeding competence; peri-device angiogenesis; invasion; thrombosis; infection; inflammatory and fibrotic remodeling; immune perturbation; altered vascular/lymphatic drainage; local-organ injury; wound-healing effects; procedural morbidity; and the possibility that capture changes shedding elsewhere. A favorable capture metric cannot compensate for a worse net metastatic or host-safety outcome.

11.2 Evidence-map discipline

For circulation and publication, each empirical claim should be traceable through an evidence map: established phenomenon → model/context supporting it → PCNN inference → untested assumption → required experiment. Cell-line, organoid, animal, observational-human, prospective-trial, and theoretical evidence should not be blended. The same separation should appear in the abstract, figures, captions, and public-facing summaries.

12. Discussion

The PCNN framework arises from a simple observation: modern oncology already contains multiple experimentally supported methods for changing the evolutionary or spatial options available to malignant populations, but these methods are usually developed as separate programs. Adaptive therapy modifies selection pressure. Synthetic lethality and dependency mapping expose conditional bottlenecks. Collateral sensitivity turns some adaptations into subsequent liabilities. Longitudinal molecular measurement can reveal state change. Engineered metastatic niches can alter where disseminating cells accumulate. Surgery, ablation, and radiation can eliminate focal disease.

PCNN proposes that the useful unit of integration is not a particular drug, gene, tumor type, or device. It is the transition: what states remain reachable after each intervention, what dependencies those states acquire, where malignant cells can physically establish, and whether the resulting configuration is observable and locally eliminable.

This perspective also changes the meaning of therapeutic success. Eradication remains the preferred endpoint when safely achievable. However, durable confinement to a bounded evolutionary region may itself be clinically valuable, and conversion of diffuse metastatic risk into focal, locally addressable disease could restore utility to local interventions. The M-Trap experiments provide a striking preclinical example of this latter principle [14], but substantial translational barriers remain.

The most speculative PCNN element is not that cancer evolves, that dependencies can be conditional, or that engineered niches can capture tumor cells; each has empirical precedent. The speculative claim is that these phenomena can be coordinated with sufficient observability, predictability, safety, and timing to form a robust closed-loop controller. That is the claim the proposed experiments are designed to test.

13. Conclusion

PCNN does not offer a universal molecular cure for cancer. It proposes a general treatment architecture: reduce malignant evolutionary freedom, exploit dependencies created by adaptation and redundancy loss, reduce dangerous spatial freedom, arrest the control mechanisms once their objectives are achieved, and eliminate locally whenever the disease has been rendered addressable. The framework is intentionally modular. A laboratory need not validate the whole system to contribute: any group capable of measuring transition probabilities, conditional dependencies, metastatic capture/egress, state observability, or local-elimination timing can test one of its edges. PCNN is a general architecture whose hypotheses must be instantiated and falsified one cancer, one dissemination route, one state transition, and one control loop at a time.

The immediate scientific question is therefore not whether PCNN should be believed. It is whether, under adversarial experimental conditions, a malignant population can be forced into a progressively smaller set of observable evolutionary and spatial states faster than it can generate new viable escape

routes. If the answer is no, the architecture should be rejected or restricted. If the answer is yes, cancer control becomes a problem of constructing and validating the controller.

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